AMENDMENTS TO THE SPECIFICATION:

Please amend the paragraph beginning at page 28, line 1 to read as follows:

$H_{48}Q$ was purified from conditioned media derived from this cell line by immunoaffinity chromatography. Purity was verified by the presence of a single band on a silver-stained SDS gel and by amino terminal peptide sequence analysis. Enzyme activity was undetectable in the purified protein as determined by the radiolabelled Eschericia coli assay (Church, W. B. et al. (2001), J. Biol. Chem. 276:33156-~~33614~~ 33164). Both mutant protein and $sPLA_2$-IIA were quantified by ELISA (Smith, G. M. et al., Br. J. Rheumatol. (1992) 31: 175). $sPLA_2$-IIA inhibitors (Church, W. B. et al) were synthesized using Fmoc (N-(9-fluoroenyl)methoxycarbonyl) solid phase chemistry without removal of side-chain protection groups prior to cleavage from the resin. Peptides were cyclised using standard peptide synthesis activation and coupling chemistry prior to deprotection (Auspep, Melbourne). The $cPLA_2$ inhibitor pyrrolidone-1 was a kind gift from Dr Michael Gelb.

Please amend the paragraph beginning at page 32, line 25, as follows:

We have previously shown that human $sPLA_2$-IIA is dose-dependently inhibited by a pentapeptide sequence comprising residues 70-74 of the native $sPLA_2$-IIA protein (^{70}FLSKY^{74}) SEQ ID NO:5 (Tseng, A., et al., (1996) J. Biol. Chem. 271:23992-23998). Because of the inherent flexibility of the linear peptide sequence, inhibition was weak in *in vitro* activity assays. We have recently designed two novel cyclic peptides (Church, W.B. et al.), cFLSYR (SEQ ID NO: 6) and a cyclic peptide where F and Y are substituted with 2-naphthylalanine (c(2NapA)LS(2NapA)R). Both have shown

significant improvement in potency over linear peptides. The potent stimulatory effect of exogenous $sPLA_2$-IIA on prostate cancer cell number was completely blocked by the $sPLA_2$-IIA inhibitor, cFLSYR (SEQ ID NO: 6) (Fig. 2B) at all concentrations tested.

Please amend the paragraph beginning at page 29, line 30 as follows:

Flow Cytometric Analysis. Cells were seeded in 25 ml flasks in conditions as described above. Following treatment, trypsinization and cell counting, LNCaP cells ($1x10^6$) were suspended in 1 mL PBS and incubated with 0.2 mL 0.4% Triton X-100 for 5 min at R/T in the presence of 50 μL of propidium iodide solution (50 μg/mL) and 20 μL of ribonuclease (10 mg/mL). DNA content per cell was measured by flow cytometry using an ~~FACScalibur~~ FACScalibur® flow cytometer and ~~CellQuest~~ CellQuest® software (Becton Dickinson, Franklin Lakes, N.J.). Statistical analysis was performed on 10,000 events per sample.

Please amend the paragraph at page 29, beginning at line 8 as follows:

RT-PCR. Total cellular RNA was isolated from LNCaP, DU145 or PC-3 cells using the ~~Trizol~~ Trizol® reagent (LifeTechnologies, Inc.). First-strand cDNA was synthesized from 5 μg of RNA with the cDNA preamplification system (Life Technologies, Inc.) using ~~SuperScript~~ SuperScript ® II reverse transcriptase and an oligo(dT) primer. This was used as the template in standard PCR reactions using ~~Amplitaq~~ Amplitaq® DNA polymerase (Perkin-Elmer Life Sciences, Boston, Mass.). Amplification products were analyzed on 2% TAE agarose gels made with ~~MetaPhor~~ MetaPhor® agarose (FMC BioProducts, Rockland, Me.) and photographed under UV

illumination. DNA ladders of 25 and 100 bp (Life Technologies, Inc.) were used as size standards. Primers were designed based on the human $sPLA_2$-IIA mRNA (NM_000300.2) deposited in the GenBank database (National Center for Biotechnology Information, Bethesda, Md.) and are as follows:

forward: 5'-TTTGTCACCCAAGAACTCTTAC-3', reverse: 5'-GGGAGGGAGGGTATGAGA-3'.

Please amend the paragraph beginning at page 30, line 29 as follows:

We searched the database of Serial Analysis of Gene Expression (SAGE) to determine the steady state mRNA levels of individual PLA_2 enzymes in prostate cancer. The cDNA libraries used for SAGE was PR317 normal prostate and PR317 prostate cancer, respectively (~~www.ncbi.nlm.nih.gov/SAGE~~ Lash *et al.*. 2000, *Genome Res.* 10:1051-1060), as both are derived from microdissected prostate tissues. We found that $sPLA_2$-IIA mRNA was 22 times higher in prostate cancer than normal prostate, whereas other members were either not expressed in the prostate libraries or unchanged in cancer. To verify the SAGE result and extend the expression analysis to androgen-independent prostate cancer (AIPC), we examined $sPLA_2$-IIA expression by immunohistochemistry in prostate cancer tissues from patients treated with androgen-ablation therapy for 3 months prior to radical prostatectomy. Cancer cells remaining in specimens following androgen-ablation therapy are regarded as being closest to AIPC, although they are confined within the prostate. Cancer specimens from patients undergoing radical prostatectomy without androgen ablation therapy served as the

control. Two antibodies were used for immunohistochemistry, and both showed the same expression pattern. In the control group, (N=50), there was weak and patchy staining in benign glands (FIGS. 1A and C.) adjacent to cancer cells and extensive staining in cancer cells (FIG. 1 C.). In the androgen-ablated group (N=25), benign glands lost their staining, whereas AIPC cells maintained $sPLA_2$-IIA expression (FIGS. 1 B and C). We also found that the extent of $sPLA_2$-IIA staining is positively correlated with the tumour grade and post-operative PSA level (data not shown). The chromosomal location of $sPLA_2$-IIA (1p35.1-36) was also found to overlap with a prostate cancer susceptibility locus CAPB (Gibbs *et al* (1999) Am. J. Hum. Genet. 64:776-787). No difference was found in immunohistochemical staining for $cPLA_2$-α between normal and cancer cells irrespective of androgen status (data not shown).